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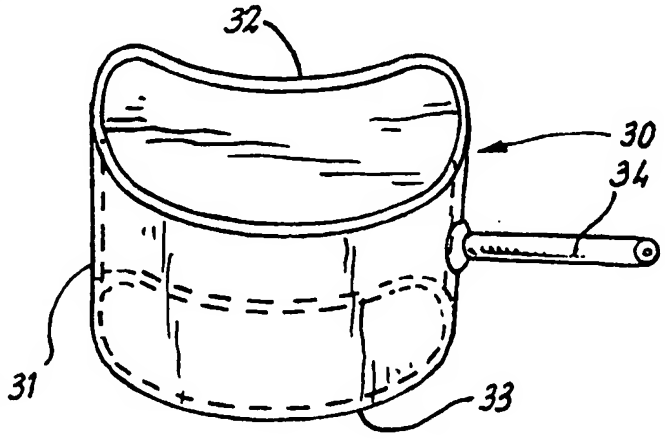
(54) Title: SURGICAL RESTORATION OF AN INTERVERTEBRAL DISC



(57) Abstract: A means for the surgical restoration of an intervertebral disc alternatively comprising a polymeric or polymerisable biocompatible material and a means of introducing said material into the internal cavity of said intervertebral disc, wherein the introduction of said material into the internal cavity facilitates at least a partial restoration of the height of said intervertebral disc; or an expandable sac (30) formed from a first biocompatible material, the sac having an entry port (34), and a second biocompatible material for introduction into the expandable sac via the entry port, the expandable sac (30) being of suitable size and shape so as to be insertable into the internal cavity of the intervertebral disc, whereby insertion of the expandable sac (30) into said internal cavity, expansion of the expandable sac (30) and introduction of the second biocompatible material into expandable sac results in at least a partial restoration of the height of the intervertebral disc.

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SURGICAL RESTORATION OF AN INTERVERTEBRAL DISC

The present invention relates to a means for surgical restoration of an intervertebral disc of the spine.

It is well established that degeneration of the intervertebral discs of the spine leads to the great majority of painful back syndromes and other debilitating conditions in man. The intervertebral disc is a structure which resides between the adjacent vertebrae and which consists of a soft nuclear material known as the nucleus pulposus contained within a cylindrical ligamentous ring known as the annulus fibrosus which is attached to the vertebral body above and below. The front of the disc is bounded by the anterior longitudinal ligament while the rear portion is bounded by the posterior longitudinal ligament.

Rupture of the annulus fibrosus with associated loss of material from the nucleus pulposus is a fairly common occurrence which is often referred to as "slipped disc". The extruded material commonly bears against nerves which are exiting the spinal column through the foramen or apertures between adjacent vertebrae and is associated with irritation and on occasion with scar formation. This generally leads to painful and debilitating conditions. In recent years, surgical procedures have been developed to remove the offending extruded material which in any event may shrink and detach over a period of time.

Associated with loss of material from the nucleus as well as other causes is a reduction in the height of the intervertebral disc and an accompanying bulging of the fibrous annulus of the disc which in turn leads to further complications. It will be appreciated that the term "height" as used herein refers to the dimension of the intervertebral disc substantially along the longitudinal axis of the spine. In the

first place, the bulging annulus may itself impinge on the nerves exiting through the foramen between the adjacent vertebral bodies or it may in other cases force the posterior longitudinal ligament to impinge on the dura mater surrounding the spinal column and hence apply pressure to the nerves of the spinal column. Additionally, the resulting reduction in the distance between adjacent vertebral bodies may reduce the size of the apertures through which the nerves exit, thereby causing pressure to be applied to the nerves passing through the apertures.

The reduction in disc height may further induce an inward buckling of the ligamentum flavum causing this structure to impinge on the posterior surface of the dura mater, again leading to pain and discomfort. The ligamentum flavum blends with the capsule of the facet joint anteriorly, and infolding of the ligamentum flavum impinges on the structures in the superior and inferior notches of the foramen and the isthmus of the foramen. The stenosis or pinching effect which causes pain when applied to the nerves may also act on the surrounding vasculature of the nerves serving the arms, legs or trunk. The embarrassment of blood flow causes congestion of the nerve surrounding tissues and a decrease in oxygen supply to the nerve with painful symptoms generally referred to as claudication, and also to loss of function. Finally, the reduction in separation of the adjacent intervertebral bodies may cause increased contact pressure between other surfaces of the adjacent vertebral bodies such as facet joints which may again lead to discomfort and pain through increased pressure on associated nerves. Reactions at the margin of the disc produce bone spurs which cause further impingement on the neural structures in the presence of settlement.

It is clear that in some cases an alleviation of symptoms could advantageously be achieved by full or partial restoration of the height of the degenerated intervertebral disc. This could be achieved by the introduction of new material into the reduced volume originally occupied by the nucleus pulposus.

Any material introduced into the internal cavity of the intervertebral disc must meet a number of criteria. Firstly, such material must clearly be biocompatible. It must not induce adverse reactions or exhibit any toxic effects on surrounding tissue. The material must further be capable of sustaining and distributing the considerable pressures which occur inside the disc when under load from the adjacent vertebral bodies. The material must remain in position within the annulus fibrosus and should ideally have no tendency to extrude from the internal cavity through pre-existing ruptures in the annulus fibrosus or through the aperture or apertures by means of which it was surgically introduced into the cavity. This latter requirement may be effectively accommodated by an efficient means of sealing pre-existing ruptures or a surgically formed aperture through the annulus fibrosus. An additional means of containing material within the intradiscal space will also afford an increased level of security against subsequent leakage or escape of said material from the internal cavity of the disc.

Any material introduced into the intradiscal cavity should be of a stable nature, resisting decomposition or deterioration into forms with unpredictable effects on surrounding tissue. The material should additionally have no tendency to exit from the intradiscal cavity by such effects as simple drainage through surrounding tissue or unwanted osmotic effects. It should here be noted that the

absorption and de-absorption of water into such material to an appropriate extent is generally acceptable as the original nucleus pulposus exhibits such hydrating and de-hydrating behaviour during different periods of the day.

A further important consideration is the degree of disruption of the annulus fibrosus which is required in order to introduce any material into the intradiscal cavity. It is evident that the introduction of a large solid or semi-solid object into the intradiscal space would require the formation of a large aperture in the annulus fibrosus which would considerably weaken this critical structure, potentially leading to further collapse and loss of nuclear material. Advantageously, therefore, the material introduced should be introduced through one or more minimal apertures which may be formed surgically in the annulus fibrosus for this purpose and which may, if desired, be located at the site of an existing rupture.

It is an object of the present invention to provide a means for the surgical restoration of an intervertebral disc.

According to a first aspect of the present invention therefore there is provided a means for the surgical restoration of an intervertebral disc, said means comprising a polymeric or polymerisable biocompatible material and an introducing means for introducing said material into the internal cavity of said intervertebral disc, wherein the introduction of said material into the internal cavity facilitates at least a partial restoration of the height of said intervertebral disc.

The polymeric or polymerisable biocompatible material may comprise any suitable material. Preferably, the polymeric or polymerisable biocompatible

material is hydrophilic. The material may be expandable, for instance upon hydration or polymerisation thereof.

The materials favoured for introduction into the internal cavity of the intervertebral disc are cross-linked hydrophilic materials formed typically from methacrylate esters such as, for example, hydroxyethyl methacrylate. The material may, alternatively, be formed from vinyl esters such as, for example, vinyl pyrollidone or from combinations of such esters and may also incorporate salts such as sodium methacrylate which are formed by the interaction of methacrylic acid residues incorporated in the polymer chains with solutions of sodium salts such as sodium carbonate. It is generally known that the presence of such salts in an hydrophilic polymer serves to increase the water uptake of the polymer with a resulting increased dimensional swell of the polymeric material.

The materials described above are at present generally in use, for example, in the manufacture of contact lenses and for certain biocompatible coatings of prosthetic elements introduced into the human body, such as arterial stents. A particular feature of such cross linked hydrophilic materials is their shape-retaining ability.

The means for introduction of the biocompatible material into the internal cavity of the intervertebral disc may take any suitable form. Suitable means include a canal or cannula of appropriate size and having a lumen of appropriate cross-section. In certain circumstances, a syringe may be used to introduce the biocompatible material into the cavity of the disc.

The present invention may be provided as an means introducing means for introduction of a polymeric or polymerisable biocompatible material ready packaged containing a portion of said material, and may be in sterile form.

In a first embodiment of the present invention, the biocompatible material may be introduced into the cavity in the form of shaped components of a particular size and shape. In this case the material may be introduced in an unhydrated form as shaped xerogel components, "xerogel" being the term for an hydrophilic polymer before hydration with water or any other hydrating agent. Following the surgical formation of an aperture through the annulus fibrosus, additional nuclear material may be excavated from the intradiscal space, if necessary, by means of laser ablation or direct surgical removal or other means known to those skilled in the surgical art such as ultrasonic emulsification similar to that used for surgical removal of the crystalline lens from the human eye, or manual extraction using instruments provided for this purpose such as punches. The shaped xerogel components may then be introduced into the intradiscal cavity, preferably in the form of a suspension of said materials in an appropriate biocompatible fluid by means of a canal with an appropriate cross-sectional form. In a particular instance, the xerogel materials may, for example, be in the form of small rods with a preferred diameter of approximately 4mm and a preferred length of approximately 10mm. In this case, the xerogel rods may be introduced into the cavity by means of a canal having a circular bore. The same canal could be used for the introduction of xerogel spheres of approximately 4mm diameter.

Upon introduction of a sufficient quantity of xerogel rods, which point may be determined, for example, by the degree of resistance to further injection of

the suspension, the aperture through which the rods were introduced may be irrigated with an appropriate hydrating solution such as physiological saline whereupon the suspending fluid will be displaced and the xerogel rods will become hydrated with an accompanying swelling as the rods hydrate into a hydrogel. It will be apparent that if the introduced rods are of a diameter similar to that of the aperture through which they were introduced into the internal cavity of the intervertebral disc, then upon swelling they will be unable to exit through the same aperture, even if they are appropriately aligned, without significant distortion which may not be achievable under the range of pressures generated inside the intradiscal cavity during normal activities.

In any event, the aperture made through the annulus fibrosus may advantageously be sealed upon completion of the procedure by means of a biological glue, such as that manufactured by Cryolife Inc., or by blood patches or other appropriate sealing means familiar to those practised in the art. Alternatively, an appropriately shaped xerogel plug may be lodged in the aperture and subsequently hydrated to provide a permanent seal.

The biocompatible material introduced into the internal cavity of the intervertebral disc, may, if desired, be provided with a small metallic component. For example, in the case of a xerogel rod, an axially placed metallic wire or a pair of thin terminal metallic discs which may have substantially the same diameter as the rod may be provided. The metallic components may be formed from stainless steel, and may be incorporated in the biocompatible material during polymerisation of a monomeric material and may serve as a useful means of

visualising the disposition and movement of the biocompatible material under x-ray.

In a second embodiment of the present invention the biocompatible material introduced into the internal cavity of the intervertebral disc may be in the form of hydrogel shaped components of similar shapes to those described in the first embodiment and again preferably suspended in an appropriate biocompatible fluid. In this case, the introduction of the hydrogel materials in their swollen form eliminates the necessity to effect the hydration of the materials *in situ*, thereby reducing the time required for the surgical procedure. The hydrogel materials may, for example, comprise shaped components formed from the esters of acrylic acids and may be hydrated with agents such as aqueous solutions or glycerol. The hydrogel shaped components may again be introduced into the intradiscal cavity by means of a canal of appropriate cross-section.

Advantageously, the canal may be provided as a sterile device containing a quantity of the biocompatible material, such as a hydrogel shaped material, ready for insertion into the disc. In this case, the possibility of obtaining an increased volume of material by swelling once the biocompatible material has been inserted into the internal cavity of the disc is limited, since the material will have already reached its swollen dimensions. It is nevertheless possible to effect some further swelling by partial or total replacement of the hydrating agent with an hydrating agent of differing composition which may be achieved by irrigating the biocompatible material with the relevant replacement hydrating agent while it is *in situ* in the internal cavity of the disc. An example of this mechanism is provided by a hydrogel containing methacrylic acid moieties. Hydration of such a hydrogel

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Advantageously, the canal may be provided as a sterile device containing a quantity of the biocompatible material, such as a hydrogel shaped material, ready for insertion into the disc. In this case, the possibility of obtaining an increased volume of material by swelling once the biocompatible material has been inserted into the internal cavity of the disc is limited, since the material will have already reached its swollen dimensions. It is nevertheless possible to effect some further swelling by partial or total replacement of the hydrating agent with an hydrating agent of differing composition which may be achieved by irrigating the biocompatible material with the relevant replacement hydrating agent while it is *in situ* in the internal cavity of the disc. An example of this mechanism is provided by a hydrogel containing methacrylic acid moieties. Hydration of such a hydrogel

with normal saline solution results, for example, in a water content of around 50% by weight of the hydrogel. Purging such hydrogel with an alkaline solution such as, for example, sodium bicarbonate solution displaces the suspending fluid and converts the methacrylic acid moieties into sodium methacrylate moieties which have a considerably greater water retention capability, leading to a water content of say 70% by weight of hydrogel with a resultant increase in size of the hydrogel shaped material.

In yet another alternative embodiment of the present invention, the biocompatible material may be formed from monomeric components within the internal cavity of the disc. This method of introduction of materials into the cavity offers several advantages. Firstly, the monomeric or pre-polymeric material being un-cross-linked or, in the case of a pre-polymer, lightly cross-linked, will exhibit viscous flow characteristics and may therefore be entered into the cavity as a single mass using a syringe-type device. Secondly, the cavity-filling characteristic of a viscous mass of this nature may be superior to the filling characteristic of numerous discreet components. Thirdly, being a single solid or semi-solid body after polymerisation, there will be no possibility of the introduced materials escaping from the cavity through a pre-existing rupture of the aperture formed for introduction of the materials. Fourthly, the polymerised and hydrated mass will form an effective seal of any such ruptures or formed aperture.

In a still further embodiment, the biocompatible material may comprise a monomeric composition containing a cross-linking agent and a polymerisation catalyst or initiator. The cross-linking agent may be a bi-functional or polyfunctional cross-linking agent. The initiator may advantageously be a

photosensitive catalyst so that the required polymerisation reaction may be initiated by irradiation of the monomer composition with light, preferably ultra-violet light, directed into the cavity by means of a fibre optic catheter. Alternatively, the monomer mixture may be one which polymerises spontaneously upon addition of a catalyst. In this case, the monomer and catalyst component may be introduced through an injection device fitted with a mixing nozzle such as that manufactured by Heraeus Kulzer and supplied for dispensing polyvinyl siloxanes for use in dentistry. Care must be taken to ensure that any heat generated during the polymerisation reaction (exotherm) is within acceptable limits and this may be achieved by control of the volume and composition of the introduced monomeric material and in particular the selection and concentration of the initiator and the consequent duration of the polymerisation reaction.

Upon completion of the polymerisation reaction, the resulting xerogel may be hydrated by continuous purging with a suitable hydrating agent such as physiological saline solution for an appropriate period of time. As the relationship between the volume of the xerogel and the resulting hydrogel will be known in all cases, appropriate allowance may be made for the swelling of the xerogel which will take place as it is hydrated into a hydrogel. The increase in dimensions upon swelling may be relied upon in this and other embodiments of the present invention to provide additional pressure contributing to the restoration of the disc height and the intavertebral separation. Small metallic particles or a radio-opaque dye or similar substance may, if desired, be incorporated in the monomer mixture in order to facilitate subsequent visualisation of the implanted material(s) under x-ray.

The monomer or pre-polymer mixture which is introduced into the intradiscal cavity may include a hydrating agent such as ethylene glycol or any other hydrating agent which permits the polymerisation of a hydrogel in its presence. In this case, a hydrogel will be formed directly upon polymerisation of the introduced material and the volume of the resulting hydrogel will be similar to that of the introduced material as the hydrogel will be effectively pre-swollen. An advantage of this embodiment lies in the ability to use alternative hydrating agents which may not be effective as post-polymerisation hydrating agents but which may be present in the first instance so that the polymer may be formed in its hydrated state. The initial hydrating agent may then be displaced by a more acceptable long-term hydrating agent in the manner described in previous embodiments of the invention. Once again, metallic or radio-opaque x-ray visualisation materials may be incorporated in the introduced material(s).

In each of the above-mentioned embodiments where the biocompatible material comprises a cross-linked hydrogel, a general composition and degree of cross-linking of the hydrogel components or mass is selected so as to provide a maximum degree of binding of the hydrating agent in order to resist as far as is possible the ejection of hydrating agent upon application of external pressure to the hydrogel. The selection of monomers, cross-linking and catalytic materials in order to provide desirable properties in relation to levels of exotherm, water-binding properties and other required properties is familiar to those skilled in the art of polymer formulation.

In addition to the introduction of a polymeric or polymerisable biocompatible material, such as a hydrogel, the restoration of the intervertebral

disc height may in certain circumstances be enhanced by the introduction of cells which have been cultured from the nuclear material present in the degenerated disc at the outset, and the present invention may therefore further comprise cells. Samples of originally present cells may be extracted from the disc which is subject to the restorative procedure using methods known to those skilled in the art and transported to an appropriate laboratory for culture growth of said cells. Upon receipt of the augmented volume of cells from the culturing laboratory, the cells may be injected into the disc cavity during or after insertion of the biocompatible material such as xerogel or hydrogel shaped components. The cultured cells will then contribute to the increased volume and may be expected to continue growth and multiplication within the spaces which exist between adjacent components of the biocompatible material. Alternatively, cells may be introduced which are derived from the bone marrow of the patient during the surgical procedure for restoration of the disc. The advantage of using such cells lies in the fact that they may be removed from the patient during the procedure for restoration of disc height, thereby eliminating the delay and subsequent operation necessary when cells have to be removed and cultured before replacement. It is believed that restoration of the normal loading of the annulus may stimulate stem cells to convert to chondrocytes and aligned fibrocytes to enhance healing and reconstitution of the annulus. The introduction of cultured cells as earlier described may be expected to produce similar healing and reconstitution effects.

The introduction of viable cells in this manner is particularly suited to the restorative means in which the biocompatible material comprises discreet components, since such introduction would not be effective in the presence of a

continuous volume of hydrogel which the cells would be unable to penetrate or, if previously introduced, to escape from.

According to a second aspect of the present invention, there is provided a method of surgical restoration of an intervertebral disc, said method comprising the following steps:

(i) forming an aperture through the annulus fibrosus of the intervertebral disc;

(ii) removing degenerated nuclear material from the internal cavity of the intervertebral disc, if required;

(iii) introducing into the internal cavity of the intervertebral disc through the aperture a polymeric or polymerisable biocompatible material using a means for introducing said material;

(iv) effecting an expansion of said material.

The method may further comprise the following step, if required:

(v) sealing the aperture.

Sealing may be achieved using any appropriate method, such as, for example, sealing with biocompatible glue.

Any means familiar to those skilled in the art may be used to form the aperture through the annulus fibrosus. Preferably, however, the aperture is formed by laser ablation of a portion of the annulus. If required, the removal of degenerated nuclear material of step (ii) may be carried out by further ablation or by any other suitable method.

The preferred biocompatible materials for use in the present aspect of the invention are those as hereinbefore described. Preferably, shaped xerogel

components are used, expansion thereof being effected in step (iv) by hydration. Preferably, hydration is achieved by continuous irrigation through the aperture with an appropriate hydrating solution. Expansion may also occur upon polymerisation of a polymerisable material.

The means of introducing the biocompatible material preferably comprises a cannula having a lumen of appropriate cross-section.

According to a further aspect of the present invention there is provided a method of surgical restoration of an intervertebral disc, said method comprising the following steps:

(i) forming an aperture through the annulus fibrosus of the intervertebral disc;

(ii) removing degenerated nuclear material from the internal cavity of the intervertebral disc, if required;

(iii) introducing into the internal cavity of the intervertebral disc through the aperture a polymeric biocompatible material using a means for introducing said material.

The method may further comprise the following step, if required:

(iv) sealing the aperture.

The polymeric material is preferably a hydrogel material, and may comprise shaped hydrogel components. The method may further comprise an additional step carried out after step (iii) and before optional step (iv), the additional step comprising further hydrating the polymeric biocompatible material by irrigating said material *in situ* with an appropriate hydrating solution, as hereinbefore described.

Further preferred features of this and subsequent aspects of the present invention are as hereinbefore described.

According to a further aspect of the present invention there is provided a method of surgical restoration of an intervertebral disc, said method comprising the following steps:

(i) forming an aperture through the annulus fibrosus of the intervertebral disc;

(ii) removing degenerated nuclear material from the internal cavity of the intervertebral disc, if required;

(iii) introducing into the internal cavity of the intervertebral disc through the aperture a mixture comprising a monomeric biocompatible material, a cross-linking agent and a photosensitive catalyst;

(iv) illuminating the mixture, thereby forming a polymeric material from said monomeric material *in situ*;

(v) hydrating the resulting polymeric material by irrigation thereof *in situ* with an appropriate hydrating agent.

The method may further comprise the following step, if required:

(vi) sealing the aperture.

The mixture in step (iv) is preferably illuminated with ultra-violet light of an appropriate wavelength, and is preferably illuminated using a fibre optic catheter. The polymeric material formed is preferably a xerogel, as hereinbefore described.

The method may further comprise a step of removing any excess hydrating agent of step (v) by irrigation with an appropriate irrigating solution.

Any of the aforementioned alternative aspects of the present invention comprising methods of surgical restoration of an intervertebral disc may incorporate the introduction into the internal cavity of the intervertebral disc cultured cells derived from cells originally present in the internal cavity or, alternatively, stem cells derived from the bone marrow of the patient undergoing the procedure.

The present invention as hereinbefore described provides an effective means for the surgical restoration of an intervertebral disc. Advantageously, however, the disc may be restored by means of an inflatable or expandable sac inserted into the internal cavity of the disc and at least partially filled with a biocompatible material such as, for example, a polymeric or polymerisable material as hereinbefore defined. Furthermore, an appropriately shaped constraint will permit preferential application of restorative forces to certain areas of the intradiscal cavity which will result in a more effective restoration of disc height without placing undue stress on the damaged wall of the annulus fibrosus.

Thus, and in accordance with a further aspect of the present invention, there is provided a means for the surgical restoration of an intervertebral disc, said means comprising an expandable sac formed from a first biocompatible material, the sac having an entry port, and a second biocompatible material for introduction into the expandable sac via the entry port, the expandable sac being of suitable size and shape so as to be insertable into the internal cavity of the intervertebral disc, whereby insertion of the expandable sac into said internal cavity, expansion of the expandable sac and introduction of the second biocompatible material into

the expandable sac results in at least a partial restoration of the height of the intervertebral disc.

The expandable sac may be inserted into the internal cavity of the intervertebral disc through an aperture formed for this purpose.

The expandable sac is preferably inflatable, and may be inflated following insertion into the internal cavity of the disc through the application of hydraulic or pneumatic pressure via the entry port, which may be a tubular entry port formed in a wall of the expandable sac. Such inflation results in an expansion of the expandable sac into the space available within the internal cavity of the disc and thereafter results in a further increase of the space within the internal cavity thereby at least partially restoring the original height of the intervertebral disc and achieving separation of the adjacent vertebrae.

The expandable sac may be spherical or cylindrical in form when expanded or may, if desired, have a three-dimensional form when expanded that approximately matches the form of the internal cavity into which it is to be introduced.

The expandable sac may be provided with walls having different thicknesses so that, for example, the cylindrical wall of a cylindrical sac may have a greater thickness than the top and bottom of the sac, such that inflation of the expandable sac will provide excess restorative force at the top and bottom surfaces.

The expandable sac may be formed from any suitable biocompatible material. Materials favoured for the fabrication of the expandable sac include hydrophilic polymers, such as those formed from acrylate esters, such as

hydroxyethyl methacrylate. Preferably, the polymers are cross-linked. The polymers may alternatively be formed from vinyl esters, such as vinyl pyrollidone, or from combinations of such esters and may also incorporate salts, such as sodium methacrylate, which are formed by the interaction of methacrylic acid residues incorporated in the polymer chains with solutions of sodium salts such as sodium carbonate. It is generally known that the presence of such salts in an hydrophilic polymer serves to increase the water uptake of the polymer with a resulting increase in the dimensional swell upon hydration of the polymeric materials. The preferred cross-linked hydrogel materials have considerable strength and may be stretched to many times their original length without breakage.

To assist in the visualisation of the expandable sac by x-ray while it is *in situ* in the intradiscal cavity, a part or the whole external surface of the sac may advantageously be coated with a thin layer of a metal such as, for example, gold, which may be sputtered onto the device before it is hydrated. Alternatively, to assist x-ray viewing of the expandable sac *in situ*, thin wire or other metallic components may be incorporated within the walls of the sac.

The entry port preferably comprises a tubular entry port which after insertion of the sac into the intradiscal cavity through a surgically prepared aperture in the annulus fibrosus extends through said aperture. Alternatively, said entry port may project inwardly into the interior of the sac. The entry port may be provided with a valve. For example, the sac may be provided with a flap secured to a wall of said sac at several points around the entry port, thereby providing an effective one-way valve, allowing application and maintenance of pneumatic or

hydraulic pressure within the sac in the manner achieved in a bellows or similar type device.

The expandable sac may be expanded by inflation with an inflating agent. This may be a gas such as air, or any other suitable biocompatible gas. Preferably, however, the sac is expanded by inflation with a liquid, such as physiological saline solution or any other suitable biocompatible liquid. A further biocompatible material may subsequently be introduced into the sac to displace the original inflating agent. For example, in one preferred embodiment, a liquid suspension of components formed from a cross-linked hydrogel similar in composition to the material of the expandable sac may be introduced. Alternatively, the further biocompatible material may comprise precursors of such hydrogel material which may be polymerised and cross-linked within the interior of the sac. Polymeric or polymerisable materials such as the materials hereinbefore described are particularly preferred for use in the present invention.

Alternatively, the second biocompatible material may comprise an un-cross-linked polymeric fluid, such as polyvinyl alcohol, such fluids being in general use in internal medical treatment of the human body. The second biocompatible material according to the present invention may be in the form of a liquid or a liquid suspension of solid components or particles which are small enough to pass through the entry port into the expandable sac.

As stated, a variety of different materials may be introduced under pressure into the interior of the expandable sac of the invention in order to sustain the expansion of the intradiscal cavity and maintain the increased disc height. Such introduction may conveniently be effected by means of a cannula attached to

the entry port of the expandable sac, which most preferably has two lumen arranged concentrically or side by side. Any material introduced to displace an initial inflating agent may be fed down one lumen while the initial inflating agent is allowed to exit from the interior of the sac through the second lumen which may be fitted, at the extra-corporeal end, with a pressure relief valve to ensure maintenance of the inflating pressure within the interior of the sac during the exchange procedure.

The second biocompatible material may be introduced into the interior of the sac in the form of shaped cross-linked hydrogel components of a particular size suspended in an appropriate biocompatible fluid such as a polyvinyl alcohol/water mixture. In this case, the components may be introduced in their unhydrated form as shaped xerogel components. Alternatively, the materials may be introduced as shaped hydrogel components in their hydrated swollen form. The material introduced into the sac may itself incorporate a metallic component or a radio-opaque dye for visualisation under x-ray illumination during and subsequent to surgery.

One preferred embodiment of the present invention provides an expandable cylindrical sac. The sac may be fabricated from cast shaped hydrogel components which are assembled in their dehydrated (xerogel) state using, for example, the monomer mixture from which the cast components are formed as an adhesive which is applied to the components in the region of their abutting surfaces and thereafter polymerised by a thermal, ultra-violet or other curing process so that the respective components are suitably bonded together to form the expandable sac. Following fabrication of the sac in the brittle xerogel form as

described, the device is preferably hydrated in an appropriate hydrating solution of, for example, physiological saline solution or sodium carbonate solution, in order to effect the transformation of the xerogel from which it is formed into a soft, flexible cross-linked hydrogel material.

Following the surgical formation of an aperture through the annulus fibrosus, additional nuclear material may, if necessary, be excavated from the intradiscal space by means of laser ablation or direct surgical removal, or other means known to those skilled in the surgical art, such as ultrasonic emulsification similar to that used for surgical removal of the crystalline lens from the human eye or manual extraction using instruments provided for this purpose such an punches. The expandable sac of the invention is then preferably attached to a tubular insertion instrument, most preferably a bi-lumen tubular instrument, and rolled or folded into a collapsed state so as to occupy the minimal cross-sectional area. Thereafter, the sac is inserted into the space prepared in the internal cavity of the intervertebral disc. Following insertion into the intradiscal cavity, the sac is preferably inflated using a pressurised biocompatible solution, such as saline, in order to achieve the desired restoration of disc height. Thereafter, the solution may be gradually displaced by a mixture of, for example, polyvinyl alcohol and water. Alternatively, the sac may be inflated in the first instance with a mixture of polyvinyl alcohol and water in which case the initial inflation with saline is not required.

In a further embodiment, the expandable sac of the invention may be in the form of a sphere. Following initial inflation with saline solution, a suspension of shaped xerogel components may be introduced into the sac interior through the

tubular insertion instrument which is as previously mentioned connected to the entry port of the sac. In a particular instance, the xerogel components may, for example, be in the form of small rods with a preferred diameter of approximately 3mm and a preferred length of approximately 10mm. In this case, the xerogel rods are preferably introduced into the sac through the lumen of a tubular insertion instrument having a circular cross-section. The same lumen may be used for introduction of xerogel spheres of approximately 4mm diameter.

Upon introduction of an initially sufficient quantity of xerogel rods, which point may be determined, for example, by the degree of resistance to further insertion, the pressure within the sac, which is maintained by the earlier mentioned pressure relief valve, may be temporarily reduced in order to achieve a packing of the discreet components. Thereafter, the pressure may be re-established and further components introduced to take up the available space. The xerogel components may now be irrigated with an appropriate hydrating solution such as physiological saline whereupon the xerogel rods will become hydrated with an accompanying swelling as the rods hydrate into a hydrogel. The irrigating liquid pumped into the interior of the sac through the same lumen as the xerogel rods can return down the second lumen of the inserting instrument thereby purging any remaining saline or xerogel suspending fluid before escape through the earlier mentioned pressure relief valve present in the extra-corporeal extension of the second lumen.

It will be apparent that if the introduced rods are of a diameter similar to that of the aperture through which they were introduced into the interior of the sac, then upon swelling, they will be unable to exit through the same aperture, even if

they are appropriately aligned, without significant distortion which may not be achievable under the range of pressures generated inside the sac interior during normal activities. If the sac is provided with a flap valve or other valve as above described, then the contents of the sac will in any event be unable to exit from the sac interior following removal of the inserting tubular instrument.

Upon completion of the sac-filling procedure, whether it be a primary filling or displacement of a primary filling with a secondary material, the aperture made through the annulus fibrosus may advantageously be sealed by means of a biological glue such as that manufactured by Cryolife Inc., or by blood patches or other appropriate sealing means familiar to those practised in the art. Alternatively, an appropriate shaped xerogel plug may be lodged in the aperture and subsequently hydrated to provide a permanent seal.

In a further embodiment of the present invention, the fluid introduced into the sac interior may be in the form of hydrogel shaped components of similar shapes to those previously described. In this case, the introduction of the swollen hydrogel components eliminates the necessity to effect the hydration of the xerogel *in situ*, thereby reducing the time required for the surgical procedure. The hydrogel shaped components may again be inserted into the sac interior by means of a two-lumen inserting instrument of appropriate cross-section attached to the entry port. In this case, the possibility of obtaining an increased volume of material by swelling once the shaped components have been inserted into the intradiscal space is limited as the hydrogel objects will have already reached their swollen dimensions.

It is nevertheless possible to effect some further swelling by partial or total replacement of the hydrating agent with an hydrating agent of differing composition which may be achieved by irrigating the hydrogel shaped components with the relevant replacement hydrating agent while they are *in situ* in the interior of the sac. An example of this mechanism is provided by a hydrogel containing methyacrylic acid moieties. Hydration of such a hydrogel with normal saline solution would result, for example, in a water content of around 50% by weight of the hydrogel. Irrigating such hydrogel with an alkaline solution such as sodium carbonate solution will convert the methyacrylic acid moieties into sodium methacrylate moieties which have a considerably greater water retention capability, leading to a water content of say 70% by weight of hydrogel with a resultant increase in dimensions of the hydrogel shaped components.

In a further embodiment of the invention, a polymeric xerogel or hydrogel may be formed from monomeric components within the expandable sac after their insertion into the intradiscal cavity. This method of introduction of material(s) into the sac interior offers several advantages. Firstly, the monomeric or pre-polymeric material being un-crosslinked or, in the case of a pre-polymer, lightly cross-linked will exhibit viscous flow characteristics and may therefore be entered into the sac as a single mass through an appropriate insertion instrument which is attached to the entry port of the sac. Secondly, the space filling characteristic of a viscous mass of this nature will be superior to the filling characteristic of numerous discreet components. Thirdly, being a single solid or semi-solid body after polymerisation, there will be no possibility of the introduced material escaping from the cavity through a pre-existing rupture or the aperture formed for

introduction of the material even upon the unlikely event of rupture of the sac. Finally, the distortion characteristics of a single mass of material under the applied forces associated with the movement of the skeleton may be superior to those provided by a suspension of discreet hydrogel components or a simple liquid.

In a still further embodiment, the biocompatible material introduced into the interior of the expandable sac comprises a monomeric composition containing a cross-linking agent and a polymerisation catalyst or initiator. The cross-linking agent may be a bi-functional or poly-functional cross-linking agent. The initiator may advantageously be a photosensitive catalyst so that the required polymerisation reaction may be initiated by irradiation of the monomer composition with, for example, ultra-violet light directed into the cavity by means of a fibre optic catheter. Alternatively, the monomer mixture may be one which polymerises spontaneously upon addition of a catalyst. In this case, the monomer and catalyst component may be introduced through an injection device fitted with a mixing nozzle such as that manufactured by Heraeus Kulzer and supplied for dispensing polyvinyl siloxane for use in dentistry. Care must be taken to ensure that any heat generated during the polymerisation reaction (exotherm) is within acceptable limits and this may be achieved by control of the volume and composition of the introduced monomeric material and in particular the selection and concentration of the initiator and the consequent duration of the polymerisation reaction.

Upon completion of the polymerisation reaction, the resulting xerogel may be hydrated by continuous purging with a suitable hydrating agent such as physiological saline solution for an appropriate period of time. As the relationship

between the volume of the xerogel and the resulting hydrogel will be known in all cases, appropriate allowance may be made for the swelling of the xerogel which will take place as it is hydrated into a hydrogel. The increase in dimensions upon swelling may be relied upon in this and other embodiments of the present invention to provide additional internal pressure contributing to the restoration of the disc height and the intavertebral separation. Small metallic particles or a radio-opaque dye or substance may, if desired, be incorporated in the monomer mixture in order to facilitate subsequent visualisation of the implanted material(s) within the sac under x-ray.

In yet another embodiment, the monomer or pre-polymer mixture which is introduced into the interior of the sac may include a hydrating agent such as ethylene glycol or any other hydrating agent which permits the polymerisation of a hydrogel in its presence. In this case, a hydrogel will be formed directly upon polymerisation of the injected material and the volume of the resulting hydrogel will be similar to that of the injected material as the hydrogel will be effectively pre-swollen. The advantage of this embodiment lies in the ability to use alternative hydrating agents which may not be effective as post-polymerisation hydrating agents but which may be present in the first instance so that the polymer may be formed in its hydrated state. The initial hydrating agent may then be displaced by a more acceptable long-term hydrating agent in the manner described in previous embodiments of the invention. Once again, metallic or radio-opaque x-ray visualisation materials may be incorporated in the injected material(s).

In each of the above-mentioned embodiments where a cross-linked hydrogel is used as the ultimate filling agent of the expandable sac of the

invention, the general composition and degree of cross-linking of the hydrogel components or mass is selected so as to provide a maximum degree of binding of the hydrating agent in order to resist as far as is possible the ejection of hydrating agent upon application of external pressure to the hydrogel. The selection of monomers, cross-linking and catalytic materials in order to provide desirable properties in relation to levels of exotherm, water-binding properties and other required properties is familiar to those skilled in the art of polymer formulation.

In addition to the introduction of material(s) into the interior of the sac for maintenance of the restored disc height, the procedure may, in certain circumstances, be enhanced by the introduction of cells which have been cultured from nuclear material present in the degenerated disc at the outset, and the present invention may therefore further comprise cells. In such cases, samples of originally present cells are extracted from the disc which is subject to the restorative procedure using methods known to the skilled in the art and transported to an appropriate laboratory for culture growth of the said cells. Upon receipt of the augmented volume of cells from the culturing laboratory, the cells may be injected into the intradiscal space before insertion of the sac or, alternatively, the cells may be injected into the interior of the sac together with the described volume-maintaining material(s).

The said cultured cells will then contribute to the increased volume and may be expected to continue growth and multiplication within the spaces which exist between the sac and the annulus fibrosus and vertebral members, or in the space between shaped hydrogel components within the sac interior. Alternatively, cells may be introduced which are derived from the bone marrow of the patient

during the surgical procedure for restoration of the disc. The advantage of using such cells lies in the fact that they may be removed from the patient during the procedure for restoration of disc height, thereby eliminating the delay and subsequent operation necessary when cells have to be removed and cultured before replacement. It is believed that restoration of normal loading of the annulus may stimulate stem cells to convert to chondrocytes and aligned fibrocytes to enhance healing and reconstitution of the annulus. The introduction of cultured cells as earlier described may be expected to provide similar healing and reconstitution effects.

The introduction of cultured cells or bone marrow stem cells into the sac interior in this manner is particularly suited to the restorative means in which the second biocompatible material comprises discreet components, as the introduction of cells would not be as effective in the presence of a continuous volume of hydrogel which the cells would be unable to penetrate.

According to a further aspect of the present invention there is provided a method of surgical restoration of an intervertebral disc, said method comprising the following steps:

(i) forming an aperture through the annulus fibrosus of the intervertebral disc;

(ii) removing degenerated nuclear material from the internal cavity of the intervertebral disc, if required;

(iii) inserting an expandable sac formed from a first biocompatible material into the internal cavity of the intervertebral disc through the aperture, the sac having an entry port and being in a collapsed state;

(iv) inflating the expandable sac by introducing into the sac via the entry port a second biocompatible material.

The method may further comprise one or more of the following optional subsequent steps:

(v) displacing the second biocompatible material with a further biocompatible material;

(vi) closing the entry port of the expandable sac; or

(vii) sealing the aperture.

Any means familiar to those skilled in the art may be used to form the aperture through the annulus fibrosus, such as a laser probe or trephine. If required, the removal of degenerated nuclear material of step (ii) may be carried out by further ablation or by any suitable method.

The expandable sac is preferably as hereinbefore defined, and is preferably inserted into the internal cavity of the intervertebral disc by means of a tubular inserting instrument having one or more lumen of appropriate cross-section.

The preferred second biocompatible materials for use in the present aspect of the invention are those as hereinbefore described. The expandable sac may be inflated using an initial inflating agent comprising a biocompatible gas or any other suitable biocompatible material as hereinbefore described.

The initial inflating material may optionally be displaced with a further biocompatible material, in accordance with optional step (v).

If required, closure of the entry port of the expandable sac may be achieved with a suitable closure device or biocompatible glue.

The entry port may be provided with an extension member in order to aid the introduction of the biocompatible material(s). If present, the extension member may be removed after use by excision or other commonly used surgical procedures.

The aperture may be sealed, if necessary, using any appropriate method, such as, for example, sealing with biocompatible glue.

In certain embodiments of the invention, for example when a xerogel material is introduced into the expandable sac as a biocompatible material, a further step of hydrating said material *in situ* may be included. Preferably, this comprises the irrigation of the sac with an appropriate hydrating agent.

In a case in which an already hydrated material, such as a hydrogel, is introduced onto the sac, it may be desirable to include a further step of re-hydrating the hydrated material *in situ* with an appropriate re-hydrating solution.

According to a further aspect of the present invention there is provided a method of surgical restoration of an intervertebral disc, said method comprising the following steps:

(i) forming an aperture through the annulus fibrosus of the intervertebral disc;

(ii) removing degenerated nuclear material from the internal cavity of the intervertebral disc, if required;

(iii) inserting an expandable sac formed from a first biocompatible material into the internal cavity of the intervertebral disc through the aperture, the sac having an entry port and being in a collapsed state;

(iv) introducing into the sac via the entry port a mixture comprising a biocompatible monomeric material, a cross-linking agent and a photosensitive catalyst;

(v) illuminating the mixture, thereby forming a polymeric material from the monomeric material *in situ*.

(vi) Hydrating the resulting polymeric material by irrigation thereof *in situ* with an appropriate hydrating agent.

The method may further comprise the following step, if required:

(vii) sealing the aperture.

A further step of pre-inflating the expandable sac with a biocompatible gas or liquid may be included between steps (iii) and (iv).

The mixture in step (v) is preferably illuminated with ultra-violet light of an appropriate wavelength, and is preferably illuminated using a fibre optic catheter. The polymeric material formed is preferably a xerogel, as hereinbefore described.

In a further embodiment of the invention, the mixture of step (iv) may alternatively comprise a biocompatible monomeric material, a cross-linking agent and a spontaneously acting initiator. In this particular embodiment, step (v) is omitted.

The mixture at of step (iv) may further comprise a biocompatible hydrating agent.

The method may further comprise a step of removing any excess hydrating agent of step (vi) by irrigation with an appropriate irrigating solution.

Any of the aforementioned alternative aspects of the present invention comprising methods of surgical restoration of an intervertebral disc may incorporate the introduction into the internal cavity of the intervertebral disc cultured cells derived from cells originally present in the internal cavity or, alternatively, stem cells derived from the bone marrow of the patient undergoing the procedure. The cells may be introduced either inside or outside the expandable sac.

The invention is exemplified in the accompanying drawings, in which:-

Fig. 1a is a diagrammatic cross-section of the human spine;

Fig. 1b is a diagrammatic cross-section of the human spine of Fig.1a showing the effect of a load applied to the spine;

Fig. 2 is a diagrammatic lateral view of the human spine showing a "slipped disc";

Figs 3 to 6 are diagrammatic perspective views of alternative embodiments of an expandable sac according to the present invention.

Referring to Fig. 1a, the human spine comprises vertebrae 10 with intervening intervertebral discs 11, said discs 11 comprising a soft nuclear material known as the nucleus pulpous 12 contained within a cylindrical ligamentous ring known as the annulus fibrosus 13 which is attached to the vertebral bodies above and below. The epiphysis 14 is also shown.

Fig. 1b shows the effect of a load applied to the disc 11 by the adjacent vertebrae 10. The load causes bulging of the annulus fibrosus 13 and deformation of the nucleus pulposus 12.

Fig. 2 shows the anatomy of a "slipped disc". The third lumar vertebrae 16 and sacrum 17 are shown. A normal intervertebral disc 18 can also be seen. However, a herniated disc 19 occurs when the annulus fibrosus 21 ruptures, leading to a loss of material from the nucleus pulposus 22. The herniated nucleus pulposus 22 impinges on an adjacent nerve 23, leading to irritation and possible scar formation.

Fig. 3 depicts an expandable sac 30 according to the present invention, being shaped so as to approximately match the form of the intradiscal cavity into which it is to be introduced. Wall 31 and top 32 and bottom 33 sections of the sac 30 are shown, as well as the tubular entry port 34. Inflation of the expandable sac 30 may be achieved by introducing a biocompatible material into the sac 30 via the tubular entry port 34.

Fig. 4 shows a cylindrical hydrogel sac 36 with wall 37, top 38 and bottom 39 sections and an entry port 41. The entry port 41 projects outwardly, although, as shown in Fig. 5, this may alternatively project inwardly into the interior of the sac 36.

As shown in Fig. 6, the expandable sac 46 may be substantially spherical in shape, having a seam 47 and a tubular entry port 48.

It is of course to be understood that the invention is not intended to be restricted to any of the above mentioned embodiments, details of which are given by way of example only.

CLAIMS

1. A means for the surgical restoration of an intervertebral disc, said means comprising a polymeric or polymerisable biocompatible material and an introducing means for introducing said material into the internal cavity of said intervertebral disc, wherein the introduction of said material into the internal cavity facilitates at least a partial restoration of the height of said intervertebral disc.

2. A means for the surgical restoration of an intervertebral disc according to claim 1, wherein the biocompatible material is expandable.

3. A means for the surgical restoration of an intervertebral disc according to either of claims 1 or 2, wherein the biocompatible material is hydrophilic.

4. A means for the surgical restoration of an intervertebral disc according to any of claims 1 to 3, wherein the biocompatible material comprises a cross-linked polymer.

5. A means for the surgical restoration of an intervertebral disc according to claim 4, wherein the cross-linked polymer is selected from one or more of a polymer formed from methacrylate esters and vinyl esters.

6. A means for the surgical restoration of an intervertebral disc according to either of claims 4 or 5, wherein the cross-linked polymer further comprises at least one salt that increases the water uptake of the polymer.

7. A means for the surgical restoration of an intervertebral disc according to any preceding claim, wherein the biocompatible material comprises a xerogel.

8. A means for the surgical restoration of an intervertebral disc according to any of claims 1 to 7, wherein the biocompatible material comprises a hydrogel.

9. A means for the surgical restoration of an intervertebral disc according to any preceding claim, wherein the biocompatible material comprises a suspension of discreet components in a biocompatible liquid.

10 A means for the surgical restoration of an intervertebral disc according to any of claims 1 to 3, wherein the biocompatible material comprises a material selected from monomeric and pre-polymeric materials.

11. A means for the surgical restoration of an intervertebral disc according to claim 10, wherein the biocompatible material further comprises a cross-linking agent and a polymerisation initiator.

12. A means for the surgical restoration of an intervertebral disc according to claim 11, wherein the polymerisation initiator is a photosensitive catalyst.

13. A means for the surgical restoration of an intervertebral disc according to any preceding claim, wherein the biocompatible material further comprises a hydrating agent.

14. A means for the surgical restoration of an intervertebral disc according to any preceding claim, wherein the biocompatible material further comprises cells.

15. A means for the surgical restoration of an intervertebral disc according to claim 14, wherein the cells comprise cells cultured from material present in the intervertebral disc to be restored.

16. A means for the surgical restoration of an intervertebral disc according to claim 14, wherein the cells comprise cells cultured from bone marrow of the recipient of the surgical restoration.

17. A means for the surgical restoration of an intervertebral disc according to any preceding claim, wherein the biocompatible material further comprises at least one of a metallic component and a radio-opaque dye.

18. A means for the surgical restoration of an intervertebral disc according to claim 17, wherein the metallic component is selected from metallic wire, discs and particles.

19. A means for the surgical restoration of an intervertebral disc according to any preceding claim, wherein the means for surgical restoration further comprises at least one hydrating agent.

20. A means for the surgical restoration of an intervertebral disc according to claim 12, wherein the means for surgical restoration further comprises a fibre optic catheter.

21. A means for the surgical restoration of an intervertebral disc according to any preceding claim, wherein the means for surgical restoration further comprises at least one of a biological glue and a blood patch.

22. A means for the surgical restoration of an intervertebral disc according to any preceding claim, wherein the introducing means has a lumen and is selected from a canal and a cannula.

23. A means for the surgical restoration of an intervertebral disc according to any of claims 1 to 21, wherein the introducing means comprises a syringe.

24. A method of surgical restoration of an intervertebral disc, said method comprising the following steps:

(i) forming an aperture through the annulus fibrosus of the intervertebral disc;

(ii) removing degenerated nuclear material from the internal cavity of the intervertebral disc, if required;

(iii) introducing into the internal cavity of the intervertebral disc through the aperture a polymeric or polymerisable biocompatible material using a means for introducing said material;

(iv) effecting an expansion of said material.

25. A method according to claim 24, wherein the biocompatible material is a biocompatible material according to any of claims 2 to 18.

26. A method of surgical restoration of an intervertebral disc according to claim 24, wherein the biocompatible material comprises a xerogel and expansion thereof is effected by hydration.

27. A method of surgical restoration of an intervertebral disc according to claim 26, wherein hydration is achieved by continuous irrigation through the aperture with a hydrating solution.

28. A method of surgical restoration of an intervertebral disc, said method comprising the following steps:

(i) forming an aperture through the annulus fibrosus of the intervertebral disc;

(ii) removing degenerated nuclear material from the internal cavity of the intervertebral disc, if required;

(iii) introducing into the internal cavity of the intervertebral disc through the aperture a polymeric biocompatible material using a means for introducing said material.

29. A method of surgical restoration of an intervertebral disc according to claim 28, wherein the biocompatible material comprises a hydrogel.

30. A method of surgical restoration of an intervertebral disc according to either of claims 28 and 29, wherein the method includes a further step of further hydrating the biocompatible material by irrigating said material *in situ* with a hydrating solution.

31. A method of surgical restoration of an intervertebral disc, said method comprising the following steps:

(i) forming an aperture through the annulus fibrosus of the intervertebral disc;

(ii) removing degenerated nuclear material from the internal cavity of the intervertebral disc, if required;

(iii) introducing into the internal cavity of the intervertebral disc through the aperture a mixture comprising a monomeric biocompatible material, a cross-linking agent and a photosensitive catalyst;

(iv) illuminating the mixture, thereby forming a polymeric material from said monomeric material *in situ*;

(v) hydrating the resulting polymeric material by irrigation thereof *in situ* with an appropriate hydrating agent.

32. A method of surgical restoration of an intervertebral disc according to claim 31, wherein the mixture in step (iv) is illuminated with ultraviolet light using a fibre optic catheter.

33. A method of surgical restoration of an intervertebral disc according to either of claims 31 and 32, wherein the biocompatible material comprises a xerogel.

34 A method of surgical restoration of an intervertebral disc according to any of claims 31 to 33, wherein the method includes a further step of removing any excess hydrating agent of step (v) by irrigation.

35. A method of surgical restoration of an intervertebral disc according to any of claims 24 to 34, wherein the aperture is formed by laser ablation of a portion of the annulus fibrosus.

36. A method of surgical restoration of an intervertebral disc according to any of claims 24 to 35, wherein the method comprises a further step of sealing the aperture.

37. A method of surgical restoration of an intervertebral disc according to claim 36, wherein sealing is achieved using a biocompatible glue.

38. A method of surgical restoration of an intervertebral disc according to any of claims 24 to 37, wherein the means for introducing the biocompatible material comprises a cannula having a lumen of appropriate cross-section.

39. A means for the surgical restoration of an intervertebral disc, said means comprising an expandable sac formed from a first biocompatible material, the sac having an entry port, and a second biocompatible material for introduction into the expandable sac via the entry port, the expandable sac

being of suitable size and shape so as to be insertable into the internal cavity of the intervertebral disc, whereby insertion of the expandable sac into said internal cavity, expansion of the expandable sac and introduction of the second biocompatible material into the expandable sac results in at least a partial restoration of the height of the intervertebral disc.

40. A means for the surgical restoration of an intervertebral disc according to claim 39, wherein the expandable sac is substantially spherical when expanded.

41. A means for the surgical restoration of an intervertebral disc according to claim 39, wherein the expandable sac is substantially cylindrical when expanded.

42. A means for the surgical restoration of an intervertebral disc according to claim 39, wherein the expandable sac has a three-dimensional form when expanded that approximately matches the form of the internal cavity into which it is to be inserted.

43. A means for the surgical restoration of an intervertebral disc according to either of claims 41 or 42, wherein the expandable sac comprises wall, top and bottom sections, the wall sections being of greater thickness than the bottom sections.

44. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 43, wherein the expandable sac is formed from a hydrophilic polymer.

45. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 44, wherein the expandable sac is formed from a cross-linked polymer.

46. A means for the surgical restoration of an intervertebral disc according to claim 45, wherein the cross-linked polymer is selected from one or more of a polymer formed from methacrylate esters and vinyl esters.

47. A means for the surgical restoration of an intervertebral disc according to either of claims 45 or 46, wherein the cross-linked polymer further comprises at least one salt that increases the water uptake of the polymer.

48. A means for the surgical restoration of an intervertebral disc according to any of claims 44 to 47, wherein the expandable sac is formed from a xerogel.

49. A means for the surgical restoration of an intervertebral disc according to any of claims 44 to 47, wherein the expandable sac is formed from a hydrogel.

50. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 49, wherein the expandable sac comprises a metallic component.

51. A means for the surgical restoration of an intervertebral disc according to claim 50, wherein the metallic component comprises a thin layer of a metal covering at least a part of an external surface of the sac.

52. A means for the surgical restoration of an intervertebral disc according to claim 50, wherein the metallic component is incorporated into the first biocompatible material.

53. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 52, wherein the entry port is a tubular entry port.

54. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 53, wherein the entry pot is provided with a valve.

55. A means for the surgical restoration of an intervertebral disc according to claim 54, wherein the valve comprises a flap secured to a wall of the expandable sac at several points around the entry port.

56. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 55, wherein the entry port projects outwardly from the expandable sac.

57. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 54, wherein the entry port projects inwardly into the interior of the expandable sac.

58. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 57, wherein the second biocompatible material comprises a gas.

59. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 57, wherein the second biocompatible material comprises a biocompatible material according to any of claims 2 to 18.

60. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 59, wherein a further biocompatible material is provided for displacement of the second biocompatible material.

61. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 60, wherein the means for surgical restoration further

comprises an introducing means for introducing the second biocompatible material into the expandable sac.

62. A means for the surgical restoration of an intervertebral disc according to claim 61, wherein the introducing means is selected from a canal, a cannula and a syringe.

63. A means for the surgical restoration of an intervertebral disc according to claim 62, wherein the introducing means comprises a cannula with two lumen.

64. A means for the surgical restoration of an intervertebral disc according to claim 63, wherein the arrangement of the lumen is selected from concentric and side by side.

65. A means for the surgical restoration of an intervertebral disc according to any of claims 61 to 64, wherein the introducing means is provided with a pressure relief valve.

66. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 65, wherein the means for surgical restoration further comprises at least one hydrating agent.

67. A means for the surgical restoration of an intervertebral disc according to claim 39, wherein the means for surgical restoration further comprises a fibre optic catheter.

68. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 67, wherein the means for surgical restoration further comprises at least one of a biological glue and a blood patch.

69. A means for the surgical restoration of an intervertebral disc according to any of claims 39 to 68, wherein the means for surgical restoration further comprises cultured cells.

70. A method of surgical restoration of an intervertebral disc, said method comprising the following steps:

(i) forming an aperture through the annulus fibrosus of the intervertebral disc;

(ii) removing degenerated nuclear material from the internal cavity of the intervertebral disc, if required;

(iii) inserting an expandable sac formed from a first biocompatible material into the internal cavity of the intervertebral disc through the aperture, the sac having an entry port and being in a collapsed state;

(iv) inflating the expandable sac by introducing into the sac via the entry port a second biocompatible material.

71. A method of surgical restoration of an intervertebral disc according to claim 70, wherein the expandable sac comprises an expandable sac according to any of claims 40 to 52.

72. A method of surgical restoration of an intervertebral disc according to either of claims 70 and 71, wherein the expandable sac is inserted into the internal cavity of the intervertebral disc by means of a tubular inserting instrument having one or more lumen.

73. A method of surgical restoration of an intervertebral disc according to any of claims 70 to 72, wherein the second biocompatible material comprises a biocompatible materials according to either of claims 58 or 59.

74. A method of surgical restoration of an intervertebral disc according to any of claims 70 to 73, wherein the method further comprises at least one of the following steps:

(v) displacing the second biocompatible material with a further biocompatible material;

(vi) closing the entry port of the expandable sac; or

(vii) sealing the aperture.

75. A method of surgical restoration of an intervertebral disc according to claim 74, wherein the further biocompatible material of step (v) comprises a biocompatible material according to claim 58.

76. A method of surgical restoration of an intervertebral disc according to either of claims 74 or 75, wherein either or both of steps (vi) and (vii) are achieved using a biocompatible glue.

77. A method of surgical restoration of an intervertebral disc according to any of claims 70 to 73, wherein the biocompatible material is a xerogel and a further step of hydrating said xerogel *in situ* is included.

78. A method of surgical restoration of an intervertebral disc according to any of claims 70 to 73, wherein the biocompatible material is a hydrogel and a further step of further hydrating said hydrogel *in situ* is included.

79. A method of surgical restoration of an intervertebral disc, said method comprising the following steps:

(i) forming an aperture through the annulus fibrosus of the intervertebral disc;

(ii) removing degenerated nuclear material from the internal cavity of the intervertebral disc, if required;

(iii) inserting an expandable sac formed from a first biocompatible material into the internal cavity of the intervertebral disc through the aperture, the sac having an entry port and being in a collapsed state;

(iv) introducing into the sac via the entry port a mixture comprising a biocompatible monomeric material, a cross-linking agent and a photosensitive catalyst;

(v) illuminating the mixture, thereby forming a polymeric material from the monomeric material *in situ*.

(vi) Hydrating the resulting polymeric material by irrigation thereof *in situ* with an appropriate hydrating agent.

80. A method of surgical restoration of an intervertebral disc according to claim 79, wherein the method includes a further step of sealing the aperture.

81. A method of surgical restoration of an intervertebral disc according to either of claims 79 to 80, wherein the expandable sac comprises an expandable sac according to any of claims 40 to 52.

82. A method of surgical restoration of an intervertebral disc according to either of claims 79 and 81, wherein the expandable sac is inserted into the internal cavity of the intervertebral disc by means of a tubular inserting instrument having one or more lumen.

83. A method of surgical restoration of an intervertebral disc according to any of claims 79 to 82, wherein a further step of pre-inflating the expandable

sac with a biocompatible gas or liquid is included between steps (iii) and (iv).

84. A method of surgical restoration of an intervertebral disc according to any of claims 79 to 83, wherein the mixture of step (v) is illuminated with ultra-violet light using a fibre optic catheter.

85. A method of surgical restoration of an intervertebral disc according to any of claims 79 to 84, wherein the polymeric material is a xerogel.

86. A method of surgical restoration of an intervertebral disc according to any of claims 79 to 84, wherein the mixture at step (iv) further comprises a biocompatible hydrating agent.

87. A method of surgical restoration of an intervertebral disc according to any of claims 79 to 85, wherein the method includes a further step of removing any excess hydrating agent of step (vi) by irrigation.

88. A method of surgical restoration of an intervertebral disc according to any of claims 70 to 87, wherein the method further comprises the introduction of cultured cells into the internal cavity of the intervertebral disc.

89. A method of surgical restoration of an intervertebral disc, said method comprising the following steps:

(i) forming an aperture through the annulus fibrosus of the intervertebral disc;

(ii) removing degenerated nuclear material from the internal cavity of the intervertebral disc, if required;

(iii) inserting an expandable sac formed from a first biocompatible material into the internal cavity of the intervertebral disc through the aperture, the sac having an entry port and being in a collapsed state;

(iv) introducing into the sac via the entry port a mixture comprising a biocompatible monomeric material, a cross-linking agent and a spontaneously acting initiator, thereby forming a polymeric material from the monomeric material *in situ*.

(v) Hydrating the resulting polymeric material by irrigation thereof *in situ* with an appropriate hydrating agent.

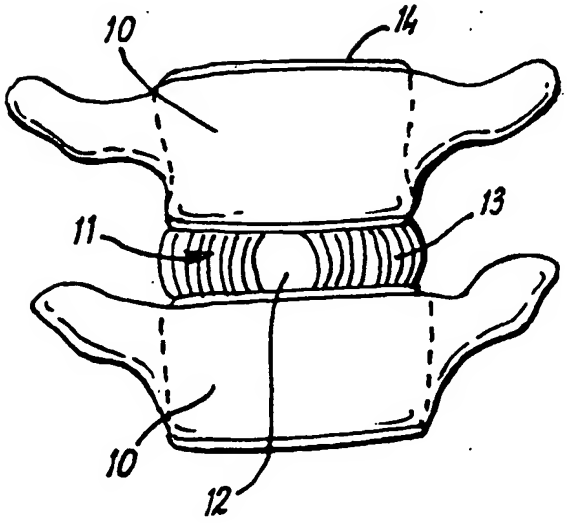

FIG 1a

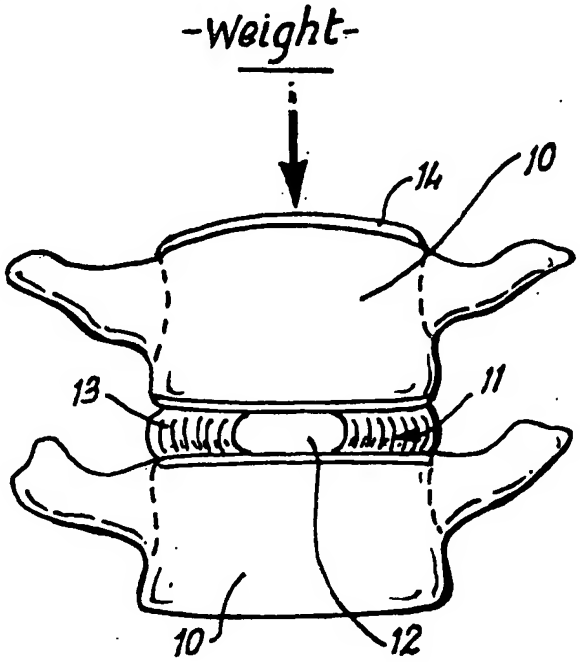

FIG. 1b

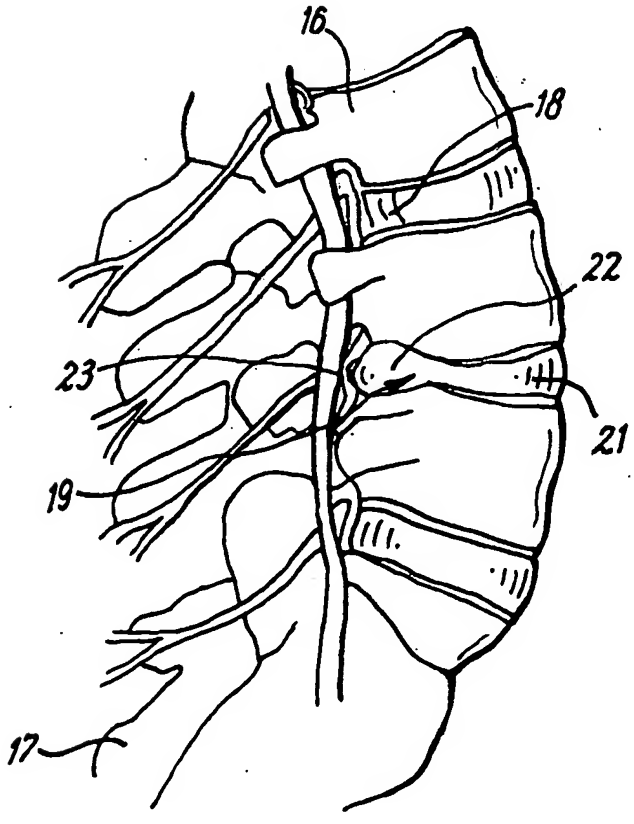

FIG. 2

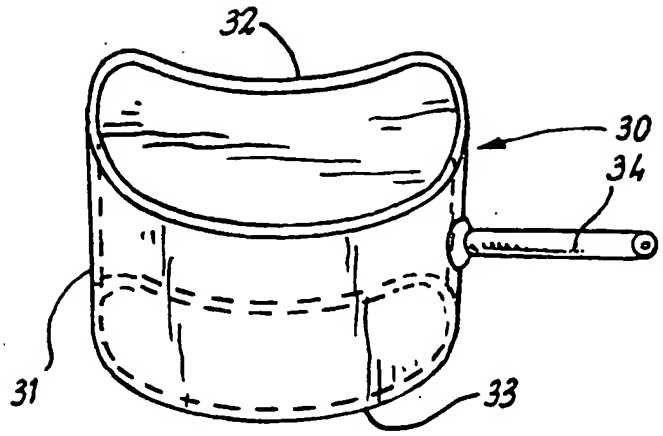

FIG. 3

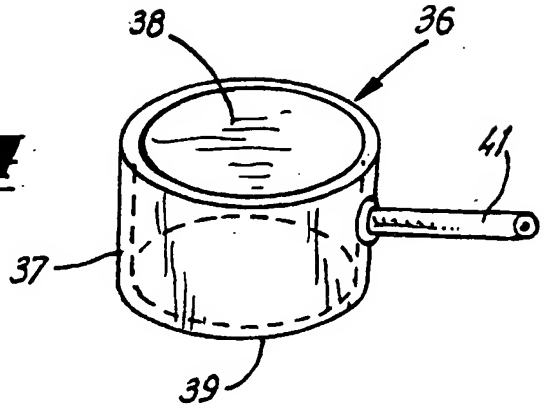

FIG. 4

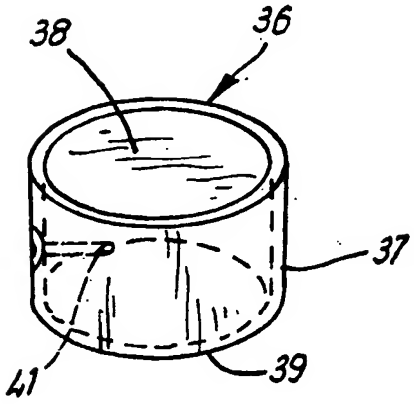

FIG. 5

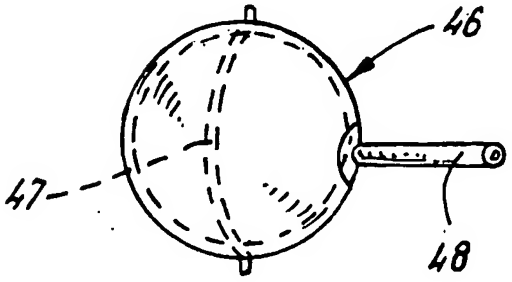

FIG. 6

INTERNATIONAL SEARCH REPORT

Int[illegible]nal Application No
PCT/GB 02/01818

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61F2/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 20939 A (ADVANCED BIO SURFACES INC ;RYDELL MARK A (US); FELT JEFFREY C (US)) 22 May 1998 (1998-05-22) abstract page 3, line 11 - line 13 page 43, line 20 -page 44, line 18 page 44, line 29 -page 45, line 2 page 45, line 19 - line 22 page 55, line 23 -page 56, line 2 page 57, line 9 - line 11 page 57, line 13 - line 29 page 69, line 14 - line 19 --- -/--	1-5, 8-12,17, 20,22, 23,39, 41,42, 44-46, 49,53, 54,56, 58-63,67

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 September 2002	26/09/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Storer, J

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 12107 A (BANKS THOMAS ;MEDGENESIS INC (US); VIDAL CLAUDE A (US); LAMBRECHT) 22 February 2001 (2001-02-22)	1-4,8, 14,21, 22,39, 41,44, 45,49, 53,56, 59,60,68
Y	page 24, line 20 -page 25, line 12 page 27, line 16 - line 18 page 28, line 13 - line 15 page 32, line 4 - line 11 page 40, line 30 -page 41, line 7 page 42, line 15 -page 43, line 2 figures 17-19	5-7,13, 19, 46-48,66
X	WO 98 56301 A (SCRIBNER ROBERT M ;REILEY MARK A (US); REO MICHAEL L (US); SCHOLTE) 17 December 1998 (1998-12-17)	1,2,17, 39-42, 53,56
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X	US 5 571 189 A (KUSLICH STEPHEN D) 5 November 1996 (1996-11-05) column 7, line 8 - line 20 column 7, line 41 - line 53 column 9, line 10 - line 13 column 9, line 49 - line 58 column 10, line 2 - line 9 column 10, line 38 - line 41 column 11, line 25 - line 37 column 12, line 11 - line 22 figures 1,2,5,8,9,53-56	1,2,14, 17,18, 22,39, 40,42, 43,50, 52,53, 55,56, 61,62
X	US 5 716 416 A (LIN CHIH-I) 10 February 1998 (1998-02-10) column 2, line 57 - line 60 column 3, line 2 - line 14 figures 1A,1B,4A-E	1,3,8, 17,18, 22,23

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INTERNATIONAL SEARCH REPORT

Int[illegible]onal Application No
PCT/GB 02/01818

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01 22902 A (STOY VLADIMIR A) 5 April 2001 (2001-04-05) page 29, line 11 - line 16 page 32, line 15 -page 34, line 2	5-7,13, 19, 46-48,66
A	page 36, line 3	1-4,8, 44,45,49

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A	WO 00 64385 A (LI MEDICAL TECH INC) 2 November 2000 (2000-11-02) the whole document	1-23, 44-49

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A	WO 97 26847 A (ADVANCED BIO SURFACES INC ;RYDELL MARK A (US); BAKER MATTHEW W (US) 31 July 1997 (1997-07-31) the whole document	39-69

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-23

Claims 1-23 refer to a means for surgical restoration of an intervertebral disc with a biocompatible material, whereby the material is polymeric or polymerisable and said means further comprises an introducing means for said material.

2. Claims: 39-69

Claims 39-69 refer to a means for the surgical restoration of an intervertebral disc with a biocompatible material, whereby said means comprises an expandable sac with an entry port to be filled with a second biocompatible material.

The common general concept is a means for surgical restoration of an intervertebral disc with a biocompatible material. This concept, however, is commonplace in the relevant state of the art (see, for example, WO-A-9820939), thus the requirement of unity according to Rule 13.1 PCT is not fulfilled. Furthermore, the means according to claim 1 does not necessarily comprise an expandable sac and the second biocompatible material refferred to in claim 39 is not necessarily polymeric or polymerisable. Indeed, these two independent claims are concerned with solving different technical problems. The subject-matter of claim 1 solves the problem of adequately filling the internal cavity of an intervertebral disc, whereas the subject-matter of claim 39 deals with the problem of generating and withstanding higher pressures within a restored intervertebral disc. Therefore, the requirements of unity of Rule 13 PCT as a whole are not fulfilled.

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ıational application No.
PCT/GB 02/01818

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 24-38,70-89
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [X] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

nformation on patent family members

Int ɔnal Application No
PCT/GB 02/01818

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte ɔnal Application No
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